UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,789	04/08/2005	Yutaka Tokiwa	SAEG 184.001APC	9374

20995 7590 03/02/2009

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
GOON, SCARLETT Y	
ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
03/02/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	10/530,789	TOKIWA ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8 December 2008 and 07 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11-17 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11-17 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8 December 2008 has been entered.

This Office Action is in response to Applicants' Amendment and Remarks filed on 8 December 2008 in which claims 1 and 13 are amended to change the scope and breadth of the claims.

Claims 1, 11-17 and 37 are pending in the instant application.

Priority

This application is a National Stage entry of PCT/JP03/13018 filed on 10 October 2003, and claims priority to Japanese patent application No. 2002-297040, filed on 10 October 2002, Japanese patent application no. 2002-353403, filed on 5 December 2002, Japanese patent application no. 2003-117973, filed on 23 April 2003, and Japanese patent application no. 2003-294543, filed on 18 August 2003. A certified copy of each foreign priority document, in Japanese, has been received. No English translation has been provided for any of the foreign priority documents.

Rejections Withdrawn

Applicant's amendment, filed 8 December 2008, with respect to the rejection of claims 1, 11-14, 16, 17 and 37 under 35 USC § 102(b) as being anticipated by WIPO WO2001/79241 to Weiss *et al.*, has been fully considered and is persuasive because the claim as amended deletes the formula that is anticipated by the compounds and methods disclosed by Weiss *et al.*

Applicant's amendment, filed 8 December 2008, with respect to the rejection of claim 15 under 35 USC § 103(b) as being unpatentable over WIPO WO2001/79241 to Weiss *et al.*, in view of Japanese publication 2001-151623 to Kiyoshi *et al.*, has been fully considered and is persuasive because the claim as amended deletes the formula that is anticipated by the compounds and methods disclosed by Weiss *et al.*

These rejections have been **withdrawn**.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 11-17 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "an alkylene group" in claims 1 and 13 renders the claims herein indefinite. An alkylene group can refer to a double bond connecting two carbon atoms,

or it can be used to refer to an alkandiyl group. Thus, in the absence of a further limiting definition in the Specification, it is unclear what is encompassed by the term “alkylene” in the claims. It is unclear whether Applicant’s intend for "alkylene” to refer to a set of double bonded carbon atoms, only alkandiyl groups, unsaturated and saturated alkane chains, or substituted or unsubstituted groups.

The recitation “by one of formulae (11) to (17)” in claim 13 renders the claims herein indefinite. It is unclear what formula (16) represents.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 1, 11-17 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are directed to a compound of formula (1) wherein Ra is as indicated in claim 1, as well as methods of making arbutin ester compounds from arbutin and compounds of formula (11) to (15) and (17).

The MPEP states that for a generic claim, the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. See MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618. Additionally, in *Carnegie Mellon University v. Hoffman-La Roche Inc.*, Nos. 07-1266, -1267 (Fed. Cir. Sept. 8, 2008), the Federal Circuit affirmed that a claim to a genus described in functional terms was not supported by the specification's disclosure of species that were not representative of the entire genus. Furthermore, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.,* 43 USPQ2d 1398.

The claims are rejected under the written description requirement for failing to disclose a representative number of species for the claimed genus.

The Guidelines for Examination of Patent Applications under the 35 USC § 112, first paragraph, "Written Description" Requirement", published at Federal Register, Vol. 66, No. 4, pp. 1099-1111 outline the method of analysis of claims to determine whether adequate written description is present. The first step is to determine what the claim as a whole covers, i.e., discussion of the full scope of the claim. Second, the application should be fully reviewed to understand how applicant provides support for the claimed invention including each element and/or step, i.e., compare the scope of the claim with the scope of the description. Third, determine whether the applicant was in possession of the claimed invention as a whole at the time of filing. This should include the following considerations: (1) actual reduction to practice, (2) disclosure of drawings or structural chemical formulas, (3) sufficient relevant identifying characteristics such as complete structure, partial structure, physical and/or chemical properties and functional characteristics when coupled with a known or disclosed correlation between function and structure, (4) method of making the claimed invention, (5) level of skill and knowledge in the art and (6) predictability of the art. For claims 1, 11-17 and 37, each of these factors has been considered, with the most relevant factors discussed below. For each claim drawn to a genus, each of these factors is to be considered to determine whether there is disclosure of a representative number of species that would lead one skilled in the art to conclude that applicant was in possession of the claimed invention. Where skill and knowledge in the art is high, adequate written description would require fewer species to be disclosed than in an art where little is known; further, more species

would need to be disclosed to provide adequate written description for a highly variable genus.

First, what do the claims as a whole cover? Claim 1 and dependent claims 11, 12 and 37 are directed to an arbutin ester compound having a structure of formula (1). Claims 13 and dependent therefrom is directed to a process for producing an arbutin ester compound from compounds of formulas (11) to (15) and (17). Dependent claims 14-17 further limit the process steps.

Second, how does the scope of the claims compare to the scope of the disclosure? The variables R_1 and R_2 are claimed broader than what is supported in the disclosure. The claims are drawn to a genus of compounds of the formula (1) and methods for making such compounds, but the disclosure only provides a very limited subset of species for the compounds of formula (1), (11) to (15) and (17). Furthermore, the specification discloses that the alkylene group has 1 to 16, and preferably 2 to 8, carbon atoms.

Third, the factors need to be considered, with the most relevant factors discussed below.

Reduction to Practice: The compounds reduced to practice are disclosed in Example 1-1 and Table 1-1, wherein R_1 in $R_1C(CH_3)=CH_2$, R_1-$C(CH_3)_3$ all represent a single bond, R_1 in R_1-$CH=CH_2$ represents either a single bond or octylene group, and R_1 in R_1-$COOCH=CH_2$ represent a butylene group. No other substituted or non-substituted, branched, or linear alkylene groups, or any arylene groups are shown for

R_1. Additionally, no representative examples are shown for an arbutin ester compound of formula (1) wherein R_a is R_1-COOH and R_1-COO-R_2.

Disclosure of Drawings or Structural Chemical Formulas: The only disclosure, in addition to the species reduced to practice, is in the form of lists of possible optional substituents for R_1 and R_2, or as lists of possible compounds for formulas (11) to (15) and (17), which can be coupled with arbutin to make the arbutin ester compound. This type of disclosure is not viewed to be a representation of any of the species it encompasses. A "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species. MPEP 2163.I.A. and *Fujikawa v. Wattanasin*, 93 F. 3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996). Therefore, there is no disclosure of species (e.g. by disclosure of structural/chemical formulae) in addition to those reduced to practice.

Method of Making the Claimed Invention: The disclosure provides an enzymatic synthesis for compounds disclosed in Example 1-1 and a chemical synthesis using 4-pyrrolidinopyridine for compounds disclosed in Example 1-3 and Table 1-2. Several other examples also provide for the synthesis of the same compounds using different enzymes or chemical reagents, but no other compounds were synthesized.

Level of Skill in the Art and Knowledge in the Art: The level of skill in the art is high, about that of a Ph.D scientist with several years of experience.

Thus, having analyzed the claims with regard to the Written Description guidelines, it is clear that the specification does not disclose a representative number of

species for the arbutin ester compounds of formula (1) or the compounds of formulas (11) to (15) and (17). Thus, one skilled in the art would be lead to conclude that Applicant was not in possession of the claimed invention at the time the application was filed.

Scope of Enablement

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising 6-O-(10-undecylenoyl) arbutin for inhibiting tyrosinase, does not reasonably provide enablement for a composition comprising any compound of formula (1) for inhibiting tyrosinase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

All of the *Wands* factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected invention is drawn to a composition that inhibits tyrosinase comprising, as an active ingredient, at least one of the arbutin ester compounds according to claim 1.

Relative skill of those in the art: The relative skill of those in the art is high.

Amount of guidance/Existence of working examples: The specification provides working examples for a small set of the compounds shown to have tyrosinase inhibitory activity. These compounds include 6-O-(10-undecylenoyl) arbutin, trehalose undecylenic acid ester, undecylenic acid, sucrose undecylenic acid ester, trehalose diundecylenic acid ester, treholose oleate and arbutin. Of the compounds disclosed to have been tested, only one compound, 6-O-(10-undecylenoyl) arbutin, falls within the scope of the arbutin ester compounds according to claim 1.

State of the prior art/Predictability or unpredictability of the art: Based on the one example of an arbutin ester that exhibits tyrosinase activity, 6-O-(10-undecylenoyl) arbutin, it is unlikely that a skilled artisan would predict that all the compounds that meet the limitations of claim 1 would also successfully inhibit tyrosinase. Furthermore, the one arbutin ester tested, 6-O-(10-undecylenoyl) arbutin, has different functional groups, and thus properties, than the compounds of claim 1. If esterification of the 6-hydroxyl group plays a role in tyrosinase inhibition as Applicants indicate (paragraph 0239 of published application), it is likely that these groups will render the arbutin ester to have different tyrosinase inhibitory activity when compared to 6-O-(10-undecylenoyl) arbutin.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully describe the genus, visualize, or recognize, the identity of the members of the genus by structure, formula, or chemical name, of the claimed subject matter, as discussed above in *University of California v. Eli Lilly and Co*. Hence, in the absence of fully recognizing the identity of the members of the genus herein, one of ordinary skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the pharmaceutical compositions herein.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the use of the claimed compounds for inhibiting tyrosinase, as recited in the instant claims.

Genetech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors as discussed above, e.g., the amount of guidance provided and the predictability of the art, to practice the claimed invention

herein, a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

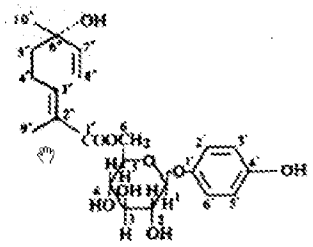
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 11 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by journal publication by Takido *et al.* (PTO-892, Ref. U).

Takido *et al.* disclose a compound called phlebotrichin. Phlebotrichin, compound (2), is a phenolic glucoside and its structure is shown in Figure 1 (p. 224) and below. Phlebotrichin was extracted from fresh leaves of *Viburnum phlebotrichum* with methanol, further chromatographed on silica gel using ethyl acetate, and then recrystallized in ethyl acetate (p. 324, column 1).



It is noted that Takido *et al.* do not teach that phlebotrichin inhibits tyrosinase, or as an external preparation for the skin. However, the recitations “a composition that inhibits tyrosinase” in claim 11 or “external preparation for the skin” in claim 12 are

considered to be an "intended use" of the composition, and is therefore not given any patentable weight. Applicant is requested to note that the "intended use" of a composition will not further limit the claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same ingredients in an effective amount, as that instantly claimed. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161.

Thus, phlebotrichin and solutions containing the phlebotrichin, disclosed by Takido *et al.*, anticipates claims 1, 11 and 12.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13-17 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over journal publication by Takido *et al.* (PTO-892, Ref. U) as applied to claims 1, 11 and 12, further in view of WIPO publication WO2001/79241 to Weiss *et al.* (IDS dated 1 July 2005), in view of publication by Kiyoshi *et al.* (of record).

The teachings of Takido *et al.* were as disclosed above in the claim rejections under 35 USC § 102. Takido *et al.* do not disclose methods for the synthesis of phlebotrichin.

Weiss *et al.* teach biologically active glycoside esters, methods for their production and the use of these compounds in cosmetic or pharmaceutical preparations. The biologically active glycoside ester is made by reaction at the primary hydroxyl group of the sugar/glycoside (p. 2, paragraph 8). Preferred monosaccharide glycosides include glucose and arbutin (p. 2, paragraphs 13-14). Suitable fatty acids for esterification include stearidonic acid and 6,9,12,15-octadecatetraenoic acid (p. 2, paragraph 13).

The esterification reaction for the production of the glycoside ester is preferably carried out in the present of a lipase (p. 4, paragraph 4). Suitable enzymatic catalysts for esterification include lipases from Candida antarctica, Candida rugosa, Geotrichum candidum, aspergillus niger, penicillum roqueforti, rhizopus arrhizus and Mucor miehei (p. 4, paragraph 5). To purify the glycoside esters from the enzymatic reaction, an aqueous two-phase extraction procedure with organic solvents such as hexanes, cyclohexane, THF, or diethylether, is employed (p. 4, paragraph 10).

The glycoside ester compounds can be made into cosmetic preparations such as shampoos, lotions, creams, gels, etc. (p. 5, paragraph 1). In addition to the glycoside ester active ingredient, the cosmetic or pharmaceutical composition can further be combined with other active substances, together with one or more inert carriers or diluents (p. 5, paragraph 3).

The synthesis for esterification of arbutin with stearidonic acid is described in Example 3 (p. 5, last paragraph). The reaction is catalyzed with Lipase B from Candida antartica in the presence of molecular sieves, and was complete in 48 hours.

It is noted that Weiss *et al.* do not explicitly teach that the esterification reaction is carried out while performing a dehydration treatment. However, the procedures for the synthesis of the glycoside esters, disclosed by Weiss *et al.*, involve the use of molecular sieves. As evidenced in the technical bulletin by Gordon *et al.* (of record), molecular sieves are well-known for their drying capacity and are considered a general-purpose drying agent.

Kiyoshi *et al.* teach the preparation of a skin lotion obtained by formulating an acylated derivative of glycosyl-L-ascorbic acid with silicone oil. An acyl ester can be introduced onto glycosyl-L-ascorbic acid via a chemical reaction (p. 3, section 0009) or an enzymatic reaction (p. 4, section 0011). In the case of a chemical reaction, acylating agents that can be used include an acid or acid halide, an anhydride, or an acid ester (p. 3, section 0009). The reaction is generally performed to the exclusion of water, usually in organic solvents such as pyridine, dimethylsulfoxide, and dimethylformamide (p. 4, section 0010). The reaction proceeds regioselectively onto the 6-OH group of the glycosyl moiety. In the case of an enzymatic reaction, a lipase is generally used as the catalyst (p. 4, section 00110). Upon completion of the reaction, the product can be purified by salting out, dialysis, filtration, concentration, fractional precipitation, liquid extraction, or chromatography (p. 5-6, section 0012).

In their examples, Kiyoshi *et al.* describes the synthesis of 2-*O*-α-D-monoglucopyranosyl-6-*O*-octanoyl-L-ascorbic acid. First, 2-glucosylpyranosyl-L-ascorbic acid is dissolved in pyridine. Next, a solution of caprylic anhydride in pyridine is added to the glucosylpyranosyl-L-ascorbic acid solution and the reaction is allowed to

proceed for 165 minutes at room temperature. The reaction is stopped by the addition of methanol.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Takido *et al.*, concerning phlebotrichin, a phenolic glucoside, with the teachings of Weiss *et al.*, regarding biologically active glycoside esters of arbutin or other monosaccharides, methods for their production and the use of these compounds in cosmetic or pharmaceutical preparations, with the teachings of Kiyoshi *et al.*, regarding the preparation of a skin lotion obtained by formulating an acylated derivative of glycosyl-L-ascorbic acid, synthesized either chemically or enzymatically (using a lipase), with silicone oil. Since Weiss *et al.* teach that the glycoside ester compounds have enhanced absorption and penetration properties, and the compound taught by Takido *et al.* is an arbutin glycoside ester, one would have been motivated to develop methods for the synthesis of phlebotrichin. Furthermore, it is noted that Kiyoshi *et al.* do not teach arbutin ester compounds as is taught by Weiss *et al.* and Takido *et al.* However, as Kiyoshi *et al.* and Weiss *et al.* both teach the esterification of the primary hydroxyl group of a glycoside using an enzymatic method that employs a lipase and Weiss *et al.* further teach that the glycoside ester compounds have enhanced absorption and penetration properties in cosmetics (p. 2, paragraph 6), one would have been motivated to search for possible avenues of synthesis of these biologically active glycoside esters as a means to optimize yield and production conditions.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/SCARLETT GOON/
Examiner
Art Unit 1623